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L20: Entry 23 of 23 File: USOC Oct 28, 1947

DOCUMENT-IDENTIFIER: US 2429694 A
TITLE: Method and equipment for indicating the water content of a gas

Title (1):
Method and equipment for indicating the water content of a gas

OCR Scanned Text (4):
2,429,694 3 Instead of having the gaS in the containing cyl- inder at superatmospheric pressure, it may be at norinal or sub-atmospheric pressure and the flow of the gas through the testing equipment may be effected by suction on the exit end or by 4other 5 means such as a pump or blower. A number of compo4nds are known which change color on exposure to water-for example, some of the salts of copper, of nickel, and of cobalt. Thus, anhydrous cupric sulfate, which 10 is white, is converted to the pentahydrate, which is blue, on exposure to water. The brown an- hydrous nickel chloride is similarly converted to the green hexahydrate. Such compounds may be used in the testing of gases containing relatively 15 large amounts of water, by means of the appara- tus and procedure herein set forth, but under most circumstances there is no particular ad- vantage in doing so. 20 In the testing of gases containing very small amounts of water-e. g. with dew points well be- low O' C., much more sensitive compounds or agents are required if the testing is to be accom- plished within a reasonable length of time. It is found, in accordance with the present invention, 25 that the compounds or reaction products of Grignard reagents with certain ketones are espe- cially suited to this purpose. The ketones pre- ferred for this purpose are of the benzophenone series, and may be represented by the formula: 30 R RI 35 wherein R is eith6r hydrogen, in which instance the ketone is benz(>Phenone (2) 40 C II 0 or a dialkyl amino group R'2N-, in which instance the ketone is a tetraalkyl-p,p'-diamino benzo- 45 phenone (3) R I2N] R12 _C 50 The four alkyl groups R' may be alike or different. Particularly useful in the present invention is a member of this latter group of cor-ripounds (3) 55 wherein each R' is a methyl group-i. e. M-ichler's ketone or tetramethyl-p,p'-diamino benzophe- none: (4) (CH3)2N- (CH3)2 00 ici v A Grignard reagent is any one of a grgup of organic magnesium compounds having the 65 formula: (5) R"Mgx wherein R" is an organic radical and X is a hal- ogen. 70 The exact mechanism of the reaction between the ketone and the Grignard reagent, and of the change from colorless to colored form induced by the presence of water, is no@L, known, but the knowledge thereof is not necessary to an uri-der- 75 4 standing of the present invention. Apparently, however, these two compounds react to form the reaction product: (6) R I c omgx when benzophenone is the ketone, or (7) R12N R" R'2 I c 1 omgx when the ketone is a tetraalkyl-p,p'-diamino benz6phenone; and each of these products rearranges itself in the presence of traces of water to form a product of different color. A related group of compounds which is also useful in carrying out the present invention is that obtained by reacting a metal alkyl with a benzophenone of the type represented by Formula 1. An example is the reaction product of Michler's ketone and diphenyl magnesium. An example of the preparation of the reacti-on product, using methyl magnesium iodide as the Grignard reagent and Michler's ketone as the ketone, is as follows: 2 grams of Michler's ketone, which had been dried to constant weight at 110' C., was dissolved in 100 cc. Of benzene distilled in sodium (to remove all traces of water) To this was added slowly methyl magnesium'iodide (CH3MgI) solution, made by reacting 14.7 g. of magnesium turnings

with 54.6 g. of methyl iodide in the presence of 200 cc. of dilautyl ether in accordance with kn(>wn methods, and under strictly anhydrolis conditions. An orange precipitate appeared c-n addition of the first few cc. of methyl magnesiurri iodide solution; this precipitate dissolved o-n further addition, and the final product was a cle,.tr, pale yeilow solution. This was stored in darkness and out of contact with the atmosphere and any other sources of water vapor. The same procedure is followed wlien using other Grignard reagents and other ketones of the class described-@-allowance of course being made for their differences in molecular weights. The reaction Product Prepared in accordance with the foregoing example changes from pale yellow (or nearly colorless) to blue, on exposure to water. That prer-ared similarly but with ethyl magnesi-um L-romide instead of methyl magnesium iodide as the Grignard reagent turns from colorless to green on exposure to water, while when phenyl magnesium iodide is the Grignard reagent, the reaction Product changes from yellow to dark blue-green. When the ketone is benzophenone and the Grignard reagent is phenyl magnesium iodide the change is from color,ess to reddish brown. These reaction products differ sufficiently in water-sensitivity and other properties to permit selection of a particular one of them for a particular set of conditions. For example, the reaction product based on ethyl magnesium bromide is more water- sensitive than that based on methyl magnesium iodide, and still more waterse-Tisitive than the two referred to above based on phenyl magnesium iodide with either ketone. It will be noted that the relative amounts of the ketone and the Grignard reagent given in the foregoing example are not mol for mol, but are

OCR Scanned Text (5):
6 h,'-gher. in Grignard reagent ' This' is considered desir,ablei in. order@ to cause the, reactiorl ta go@ sufftciently to completion in. forming the- re@ action product. A volume of, 0.05 cc. of a solution of@ the, reaction product of Michler's ketone and methyl magnesium iodide (CMMgI), prepared in, accordance, with the foregoing example-and having@ a concentration of 1 % with respect@ to. the IMehler's ketone- when spread@ on #60@ r-iesh sand, tums blue with 0.06 milligram of water, when testing ordinary cylinder oxygen at ordinary temperatures' This@ sensitivity varies with variation in conditions' For example, since the@ color reaction occurs on the surface of the solution, only@ a very smail amount of the solutlo'n need be used if it is spread out as a very7 thin film, e. g@. on the, #69, mesh sand, as indicated above. The appearance of colbr also ctepends@ to some extent upon the concentration of water in the gas being- testedhigher than ordinary concentrationsi resulting in soin,ewhat lower sensitivity and lower concentrations in higher sensitivity. The sensitivity also increases somewhat with decreased concentration of the soiution of the reacti6n compound and with decreased rate of flow. It is also sfgniflcantly increased by dispersion of the, reaction compound over an extensive surface, as described in detail hereinafter. These reaction products of'Grignard reagents@ and the ketones of Formula I are stable and ef--@ fective within a fairly wide range of conditions of temperature ancl keepi@ng time. For example, the reaction product of Mehler's ketone and CH3MgI retains effective sensitivity to water after heating to 110' C', and after cooling to -78' C., and after keeping for over six weeks at 6&9 C. When this reaction product is; used, the color change reaction has a fairly large temperatur ecoefficient-thus, it takes twice as4 long to develop the same amount of color at 01 C. a,% at 25' C., and half as long at 50' C. as at 25' C.corresponding to a 6' C. change in dew point, These facts introduce no practical difficulties, however, inasmuch as the length of the test time and other factors can be adjusted within a w[de range to balance them. At -40" C'@ the color change in the reaction product of Michler's ketone and CH3MgI is gen-. erally too slow for practical use. When testing is done at such low temperatures, it is- therefbre advisable to use a more sensitive compound such as the reactioii product of Michler'8@ keton@ and ethyl magnesium bromide, which shows the color change at -501 C. or even lower. These various reaction products are rather sensitive to light, and should accordingly be kept in the dark except during the actual preparation and testing procedures. As already indicated, the reaction product is much more effective for detecting the presence of' water when said product is spread out as a film instead of being employed as a body of liquid. In

carrying o-ut the present invention, it ha& accordingly been found especially advantageous to spread the reaction product as a thin coating over a mass of clean water-free particulate material which is either transparent or of a color (e. g. white) which does not itterfere with detection of the color change of the reaction product. Sand, glass beads or particles, quartz beads, silica geI, and glass wool or flakes, in clean, thoroughly water-free cop-dition, are suitable for use@ as such particuiate material to receive the coating of-the reaction product. Im order that the color change may@ be readily.. seen, as@ w-ell as, to permit convenient sealing. and opening, the container for the reaction product. is made of glass or like transparent 5i materl'al, conveniently in the form of a tube. Pbr most purposes@ this container may be of about 5@ mm. inside diameter and about 8-10 cm. long. It@ may be made from a clean glass tube of suitable inside, diameter, which is then sealed 10 at one end, filled w@ith the particulate material and thoroughly dried@ A measured quantity oi the, solutfon of the reaction product is then introduced, as by means of a hypodermic syringe; the other end of the tube is then sealed. Ab- 15 solutely- arihydrous conditions are maintained thr-ougliout this: f@illing and sealing procedure. A-Iteinatively-, and generally more conveniently; the kltone@ and the Grignard reagent may be kept in the form of separate solutions prior to charg@ 20@ ing, the particle-filled tube, and then mixed and 25 reacted within the tube. By introducing the Grignard reagent first, any possible traces of moisture within the tube are removed by hydrolysis, of this reagent into harmless products' The sealing may be carried out in any way such that extraneous water or other deleterious material is@ excluded and that the seals may be sufriciently readily broken or punctured. For 30@ exampie, the seals may be formed by melting the ends of the glass tube, or by plugging them with stoppera of neoprene or other composition which has no tendency to absorb or adsorb MO. This invention will now be described in greater 35@ detail with reference to the accompanying drawings,- wherein: F-ig' I represents, largely diagrammatically, the arrangement of the fundamental parts of the apparatus; 40@ Mg. 2 represents a front view, partly in section, of a particular embodiment of this invention; Fig. 3 represents a side view of the type of- embodiment shown in Eng. 2, looking in the direction of arrows 31 3 in Fig. 2, and showing in particular 45@ the positioning of the means for holding the cartridge or container for the water- sensitive compound; Fig. 4 represents a modification of the cartridge or container for the water-sensitive compound; 59 and Fig. 5 represents a holder and unsealing means for cartridges or containers of the type shown in Mg. 46 Referrin@ to Fig@ 1, IO represents a container 66@ fbr the gas to be tested, and i I represents a container for the bed 12 of particulate material coated with a substance which is color-sensitive to water. Cbmmunicating between the two containers is line 14@ The ends of container I I are provided 60@ with sealing means 16, 17, which are kept closed until the testing is to take place, thereby exclud@irg all@ extraneous moisture from bed 12. Bed 12 is conveniently segregated from sealing means 16@ 17'by wads or packings 13, 13', wwch may be 66 rn@de@ of glass wool. @vor operation, container I I is attached to line 14 by coupling 18, valve i5 is opened and sealing means 16, 17 are unsealed, whereupon gas flows from container I 0 through the apparatus ta outlet 19 ' Line 14@ should be 7,0@ c-leared of all extraneous moisture prior to such operation. Rate of ebange in color of the material in bed 12 indicates the water content of the gas being tested. Suitable marks may be placed at intervals@ along the walls of container I I to 75@ note the rate of advaneer of the leading edge of

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.erable to, determirie the time elapsed between -pas- sage @of the leading edge @of the 7changed from mark 56 to -mark 57. It should be emphasized that water @and ice m,ust not be allowed to condense upon or - within 5 the testing device. @Obviously, the@presence of any such extraneous H20 within the testing space and channels leading thereto @will spoil any-determina- ttions which are attempted. The devices shown in Figs. 4 and 5 are op- 10 er,atedin the same general manner as alt@eady out- lined, except that @instead of crushing the ends of the cartridge, these ends are punctured by the hollow top needle 171 and a similar hollow bottom needle. Thus, after thepreliminary valve setting 15 using a blank cartridge, the fresh

cartridge IZO is inserted after proper flushing, as described with reference to Figs. .2 and 3; pressure is then ap- plied to head 173 to force hollow needle 171 through plug 15 1, and the plug at the other end 20 of the same cartridge is t'hen similarly pierced and the flow of gas is e! tablished by Gpening valve mea-ns 22. The terms "water" and "'H20 " referred to here- in and in the.appended claims mean water in any ,25 of its several physical forms, unless otherwise specified. Wha@t is claimed is: 1. The method of testing a gas to determine the amount of water therein, which consists in 30 passing said gas through a water-free bed of solid, water-free Particulate material coated with the reaction product of Michler's ketone and a Grig- nard reagent, said particles being inert toward said reaction product, and maintadning said gas, 35 during its passage to and through said bed, com- pletely out of contact with water other than that contained in said gas. 2. The method of testing a gas to determine the amount of water therein, which consists in pass- 40 ing said gas through a water-free bed of solid, water-free particulate material coated with the reaction product of a Grignard reagent and a benzophenone of the formula: R- 45 c wherein P. is a member of the group consisting 50 of hydrogen and dialkyl amino, said particles be- ing inert toward said reaction product, and main- taining said gas, during its passage to and through said bed, completely out of contact with water other than that contained in said gas. 55 3. The method of ascertaining the presence of small amounts of water in an elementary atmos- pheric gas, which comprises passing said gas, in out-of-contact Yelationship with ambient fluid, through a bed of clean dry particles of solid ma- 60 terial having a surface coating of the reaction Product of Michler's ketone and a Grignard re- agent. 4. The method of ascertaining the presence of small amounts of -water in an elementary - atmos- r)5 pheric gas, which comprises passing said gas into contact with the reaction product of Michler's ketone and a Grignard reagent, in out-of-contact relationship with all extraneous water, said reac- tion product being distributed as a surface coating 70 upon clean, dry, Particulate solid material inert toward said reaction product and of a color which contrasts with the color imparted to said reaction product by water. 5. The method of determining small amounts 75 10 of waterin a gai@, which comprises passing said gas into contact vith an agent which -is colorsensitive to small amounts of water, said - agent being -distributed as an -anhydrous surface coat-ing upon clean, dr-y, particulate solid material inert toward said agent and of a color which con,trasts with the color imparted to said agent by water, and @maintaining said gas, during its passage to and through said agent and said solid material, in completely out- of-contact xelationsh@p -with extraneous water or other ambient fluid, said agent being the reaction product of a Grignard reagent -and a,benzophenone. 6. T@he - method in -accordance with claim 5, wherein sadd agent is the reaction product of a C@rignard reagent and a benzophenone of the f@ormula: R wherein R is a member of the group consisting of 4ydrogen@and dialkyl amino. 7. The method in accordance - with claim 5, -wherein said agent is the reaction product of a Grignar-d reagent @and @a tetra-alkyl-@p,p'-diamino benzophenone. 8. A testing device for use in indicating the water content of a gas, said device comprising an elongated gas- tight tube sealed at its ends, clean Particulate solid material substantially filling said tube, and a surface coating of the reaction product of a Grignard reagent and a benzophenone upon said particulate solfd material, the interior of said tube and the contents thereof being free from water, said coated particulate solid material being of a color readily distinguishable from that imparted to said reaction product by water, said tube being adapted to have said sealed ends fractured whereby the said gas may be passed therethrough for testing, said tube being transparent to permit viewing from the outside the progress of color change induced in said coating on said particulate solid material by water in said gas. 9 . A d e v i c e i n a c c o r d a n c e w i t h c l a i m 8 , w h e r e i n said benzophenone has the formula: R RI c wherein R is a member of the group consisting of hydrogen and dialkyl amino. 10. A device in accordance with claim 8, wherein said benzophenone is a tetra- alkyl-p,p'-diamino benzophenone. 11. A device in accordance with claim 8, wherein said benzophenone is Michler's ketone. 12. A device in accordance with claim 8, wherein said coated particulate solid material is spaced from each of the fracturable sealed ends of said tube by a wad of inert,

gas-transmitting packing adapted to hold said particulate solid material in position. 13. Apparatus of the character described for determining the water content of a gas, which comprises first and second holding means relatively movable toward and away from each other, each of said holding means being provided with a chamber having an opening, said two openings facing each other and each being adapted to receive and hold one end of a testing cartridge in gas-tight relationship with respect to the out-

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DOCUMENT-IDENTIFIER: US 4769216 A
TITLE: Device for detecting antigens and antibodies

Abstract Text (1):
A device for use in detecting or determining the presence of antigenic or haptenic substances or antibodies in a sample comprises a plurality of tubular or capillary elements (1, 2, 3, 4, 5, 6), each having antibodies or antigenic or haptenic substances attached to an internal surface thereof, and means (11) for causing fluids to pass simultaneously or sequentially through the plurality of capillary elements. A method and test kit for detecting and determining the presence of antigenic or haptenic substances or antibodies in a sample by the enzyme-linked immunosorbent assay technique is characterized by use of urease as the enzyme in an antibody-enzyme or antigen-enzyme conjugate, with urea being used as the enzyme substrate and the presence of ammonia being detected or determined using di-bromo-o-cresolsulfonphthalein.

Brief Summary Text (60):
The improvement now provided in these further aspects resides in the use of the particular indicator di-bromo-o-cresolsulfonphthalein, or Bromcresol Purple, as the indicator of the presence of ammonia. The production of ammonia may be readily detected by a pH shift which has been found to be best detected by the vivid colour change (yellow to purple) of Bromcresol Purple incorporated in an unbuffered substrate solution. The use of urease-urea as an enzyme-substrate system offers a number of important advantages: the substrate, being stable, may be stored ready to use; titration end points are sharp and readily visible; the enzyme is not poisoned by sodium azide and therefore test reagents may be prepared with this preservative and stored ready to use (this is not the case with Horse Radish Peroxidase (HRP), an enzyme which has been used in EIA tests previously). These factors therefore make the enzyme suitable for EIA kits intended for field use. The enzyme is commercially available at a higher specific activity than other commonly used enzyme labels and, because urease does not occur in mammalian tissues whereas other enzymes such as peroxidases, phosphatases and galactosidases may occur in such tissues, it is suitable for use in EIA tests to detect cell-associated antigens and their antibodies. Finally, the enzyme reaction may, if desired, be stopped instantly by the addition of the organo mercurial preservative Thiomersal, thus allowing storage of EIA results for later examination.

Brief Summary Text (61):
The fact that Bromcresol Purple is of particular benefit as an indicator in the methods described above is surprising, since the colour change provided by Bromcresol Purple takes place in the pH range of 5.2 to 6.8. Urease, on the other hand, has a maximum activity of pH's in the range of 7 to 8. It has, nevertheless, been found that the use of Bromcresol Purple to detect the presence of ammonia is effective in giving a complete and quite rapid colour change. In contrast, other pH indicators tested do not give a comparable colour change or exhibit a similar rapidity of reaction for a given concentration of antigenic substance, for example, snake venom. FIG. 1 of the accompanying drawings illustrates the sensitivity of Bromcresol Purple (BCP) as an indicator of the presence of ammonia produced by the action of urease on urea, when compared with the other pH indicators Cresol Red (CR), Bromthymol Blue (BTB), Chlorophenol Red (CPR) and Phenol Red (PR), all of which also provide a colour change in the pH range of 5 to 8, as set out in Table 1 below.

Brief Summary Text (62):
It will be apparent from FIG. 1, that in an unbuffered system, the pH indicators BCP, BTB and PR give linear absorbance-versus-time plots, whereas CR and CPR give curved responses. In addition BCP is much more sensitive than the other indicators and gives a marked yellow to purple colour shift which can be readily detected visually as these colours are spaced far apart in the visible light spectrum. BCP therefore provides a number of advantages as indicator for use in EIA tests involving urease when

compared to the other pH indicators which would be expected to give higher reaction rates and thus be more sensitive at the pH optimum of urease in the EIA system. Bromcresol Purple is also particularly advantageous when compared with the use of the Nessler reaction to detect the formation of ammonia, as the use of a pH indicator provides a continuous measurement of urease activity and does not destroy the enzyme as in the use of the Nessler reaction. Accordingly, the use of Bromcresol Purple is of particular advantage in performing assays using urease/urea as the enzyme/substrate system in ELISA techniques.

CLAIMS:

1. A test kit for use in detecting or determining the presence of any member selected from the group consisting of antigenic substances, haptenic substances, and antibodies in a sample by an enzyme-linked immunosorbent assay technique, which comprises:

(i) a plurality of capillary elements, each of said capillary elements having any member selected from the group consisting of antigenic substances, haptenic substances, and antibodies attached to an internal surface thereof, and means for causing fluids to pass simultaneously through said plurality of capillary elements;

(ii) an antibody-enzyme or antigen-enzyme conjugate wherein when antigenic or haptenic substances are attached to the plurality of capillary elements, the conjugate is an antigen-enzyme conjugate and when antibodies are attached to the plurality of capillary elements, the conjugate is an antibody-enzyme conjugate; and

(iii) an enzyme substrate/indicator system, wherein said capillary elements are connected in series by tubular connecting elements, and said series of elements is connected to a single means for causing fluids to pass therethrough.

2. A test kit for use in detecting or determining the presence of any member selected from the group consisting of antigenic substances, haptenic substances and antibodies in a sample by an enzyme-linked immunosorbent assay technique, which comprises:

(i) a plurality of capillary elements, each of said capillary elements having any member selected from the group consisting of antignic substances, haptenic substances, and antibodies attached to an internal surface thereof, and means for causing fluids to pass simultaneously or sequentially through said plurality of capillary elements;

(ii) an antibody-enzyme or antigen-enzyme conjugate wherein when antigenic or haptenic substances are attached to the plurality of capillary elements, the conjugate is an antigen-enzyme conjugate and when antibodies are attached to the plurality of capillary elements, the conjugate is an antibody-enzyme conjugate, the enzyme in said conjugate being urease; and

(iii) an enzyme substrate/indicator system comprising urea as the enzyme substrate and di-bromo-O-cresol sulfonphthalein as said indicator.

3. A test kit according to any one of claim 2 wherein said capillary elements are constructed of glass or plastics materials, and said member selected from the group consisting of antigenic substances, haptenic substances and antibodies are attached to the internal surfaces thereof by adsorption or covalent bonding.

4. A test kit as claimed in claim 2, wherein said capillary elements have a capacity of about 5-20

microliters.

5. A test kit according to claim 2, wherein said capillary elements are connected in series by tubular connecting elements, and said series of elements is connected to a single means for causing fluids to pass therethrough.

6. A test kit according to claim 1, wherein said single means for causing fluids to pass through said series of capillary elements comprises a syringe device having means defining a bore in fluid communication with an end of one of said series of capillary elements, and a plunger movable within said bore.

7. A test kit according to claim 2, wherein said capillary elements are mounted side-by-side in a support and in fluid communication with means defining bores within said support, and said means for causing fluids to pass through said capillary elements comprises means for simultaneously drawing fluids into and expressing said fluids out of the bores through the respective capillary elements.

8. A test kit according to claim 7, wherein individual plungers are mounted within said bores for movement relative thereto to draw fluids into and express fluids out of said bores, and said individual plungers are interconnected for simultaneous movement relative to the respective bores.

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US006171811B1

(12) **United States Patent**
Becerro De Bengoa Vallejo

(10) **Patent No.: US 6,171,811 B1**
(45) **Date of Patent: Jan. 9, 2001**

(54) **METHOD AND KIT FOR DETECTING *HELICOBACTER PYLORI***

(75) Inventor: **Ana Becerro De Bengoa Vallejo**, Madrid (ES)

(73) Assignee: **Isomed, S.L.**, Madrid (ES)

(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

(21) Appl. No.: **09/101,992**

(22) PCT Filed: **Jul. 21, 1997**

(86) PCT No.: **PCT/ES97/00184**

§ 371 Date: **Jul. 20, 1999**

§ 102(e) Date: **Jul. 20, 1999**

(87) PCT Pub. No.: **WO98/21579**

PCT Pub. Date: **May 22, 1998**

(30) **Foreign Application Priority Data**

Nov. 12, 1996 (ES) 9602383

(51) **Int. Cl.**[7] **C12Q 1/04**; C12Q 1/02; G01N 33/53

(52) **U.S. Cl.** **435/34**; 435/29; 435/975; 435/968

(58) **Field of Search** 435/34, 29, 975, 435/968

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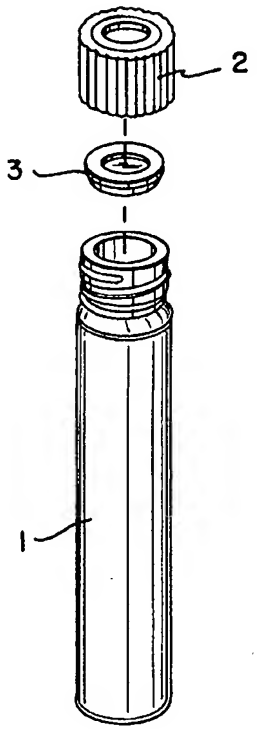
Primary Examiner—Louise N. Leary
(74) *Attorney, Agent, or Firm*—Darby & Darby

(57) **ABSTRACT**

The method is based on the carbon-13 labelled urea breath test, which comprises a) administering to the patient an aqueous solution of citric acid at pH comprised between 2 and 2.5; b) collecting a sample of the patient's breath with the object of determining the baseline content of carbon-13; c) administering to the patient a suitable amount of carbon-13 labelled urea; d) collecting a sample of the patient's breath with the object of determining the content of carbon-13 after the administration of the labelled urea; and e) analyzing the breath samples collected to determine the carbon-13 content before and after the administration of urea labelled with carbon-13. The kit has a container for the citric acid, another for the carbon-13 labelled urea, exetainers destined to containing the patient's breath, and means to blow the breath into the exetainers.

37 Claims, 1 Drawing Sheet



The urea breath test is based upon the fact that an abnormal urease activity is observed in numerous gastroduodenal diseases, particularly in those related with the presence of H. pylori, and hence, the detection of urease activity in abnormal amounts is indicative of the existence of H. pylori, and consequently, of a possible gastroduodenal pathology. Urease (urea amidohydrolase) is an enzyme which catalyses the hydrolysis of urea (carbonyldiamide) into ammonium carbonate which decomposes into carbon dioxide and ammonia. In order to carry out the urea breath test, the patient is administered urea, which is optionally labelled with carbon-13 (.sup.13 C), carbon-14 (.sup.14 C), or with nitrogen-15 (.sup.15 N), and the breath of the patient is subsequently analysed to detect the presence of products resulting from the hydrolysis of the labelled urea. The carbon dioxide labelled with carbon-13 or carbon-14, produced by the hydrolysis of the urea labelled with said isotopes, is absorbed by the blood system, transported to the lungs and is finally exhaled, making its detection possible in the breath of the patient.

DOCUMENT-IDENTIFIER: US 5094962 A
TITLE: Microporous article having a stabilized specific binding reagent, a method for its use and a diagnostic test kit

Brief Summary Text (65):
For instance, the ligand can be complexed with a water-soluble, detectably labeled (as described above) second receptor as well as with the reagent. This is generally known in the art as an immunometric or "sandwich" assay. The labels can be as described above, but are preferably radioisotopes or enzymes, and more preferably, enzymes (such as peroxidase, alkaline phosphatase, glucose oxidase, urease or .beta.-galactosidase). The receptors can be the same or different as long as they do not inhibit the complexation of ligand with the other.

Brief Summary Text (80):
Preferably, the dye-forming composition includes a leuco dye which provides a dye in the presence of hydrogen peroxide and peroxidase [for example, a triarylimidazole leuco dye as described in U.S. Pat. Nos. 4,089,747 (issued May 16, 1978 to Brushci) or a triarylmethane leuco dye as described in 4,670,385 (issued June 2, 1987 to Babb et al)]. A preferred dye-providing composition is described and claimed in copending and commonly assigned U.S. Ser. No. 136,166, filed Dec. 18, 1987 by McClune.

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US005420016A

United States Patent [19]

Boguslaski et al.

[11] **Patent Number: 5,420,016**

[45] **Date of Patent: May 30, 1995**

[54] **TEST DEVICE AND KIT FOR DETECTING HELICOBACTER PYLORI**

[75] Inventors: **Robert C. Boguslaski; Robert J. Carrico**, both of Elkhart, Ind.

[73] Assignee: **Serim Research Corporation**, Elkhart, Ind.

[21] Appl. No.: **198,236**

[22] Filed: **Feb. 18, 1994**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 856,992, Mar. 24, 1992, Pat. No. 5,314,804.

[51] **Int. Cl.**[6] **C12Q 1/58**; C12Q 1/04; G01N 21/00

[52] **U.S. Cl.** **435/12**; 435/34; 436/169; 436/808; 422/58

[58] **Field of Search** 422/56, 57, 58, 60, 422/61; 435/10, 12, 34, 805, 810; 436/169, 808, 810

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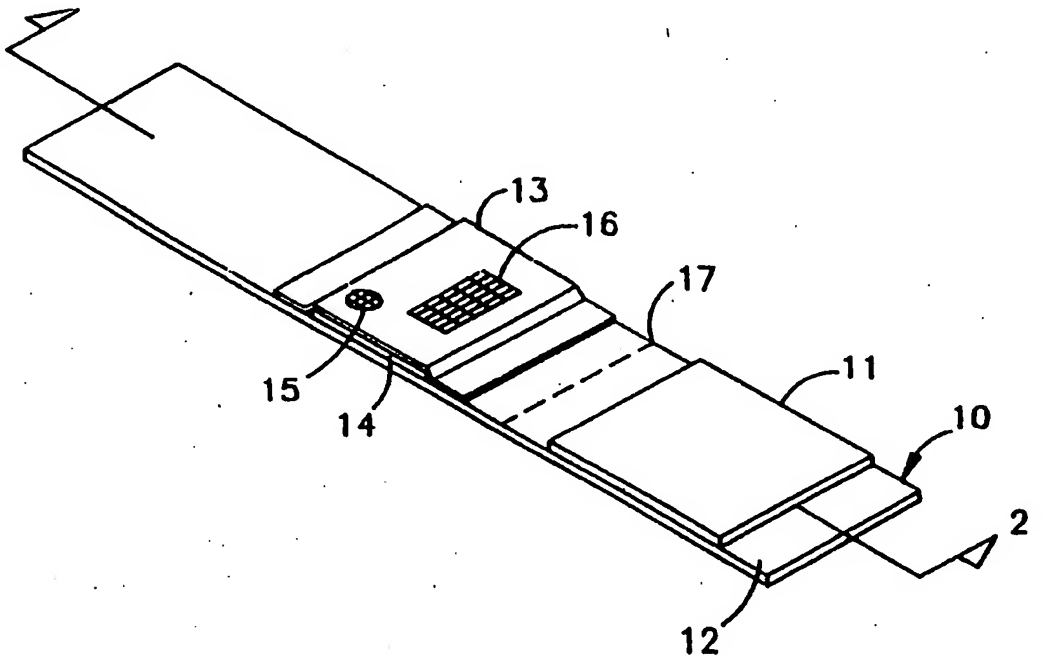
Attorney, Agent, or Firm—Baker & Daniels

[57] **ABSTRACT**

A rapid method and easy to use unitized test device is disclosed for determining the presence of *Helicobacter pylori* in a biological tissue specimen by detecting the presence of urease in the tissue. The system basically utilizes a multilayer test device for separating and optimizing the various reactions involved, i.e. the urease in the specimen with a substrate and the ammonia generated thereby with an indicator element.

15 Claims, 1 Drawing Sheet



DOCUMENT-IDENTIFIER: US 5420016 A
TITLE: Test device and kit for detecting helicobacter pylori

Abstract Text (1):
A rapid method and easy to use unitized test device is disclosed for determining the presence of Helicobacter pylori in a biological tissue specimen by detecting the presence of urease in the tissue. The system basically utilizes a multilayer test device for separating and optimizing the various reactions involved, i.e. the urease in the specimen with a substrate and the ammonia generated thereby with an indicator element.

CLAIMS:

9. A test kit for detecting urease in biological tissue specimens comprising:

A. an aqueous rehydrating solution;

B. a buffer having a pH of about from 7.0 to 9.0;

C. a substrate element comprising a matrix having therein a dried residue of urea;

D. a diffusion element comprising a membrane permeable to ammonia and impermeable to water;

E. an indicator element comprising a matrix containing a dried residue of a pH indicator having a pKa of about from 2.0 to 6.0 for detecting ammonia, the indicator element being in contiguous relationship with the diffusion element;

F. wherein a predetermined quantity of sulfamic acid sufficient to react with ammonia to produce a desired sensitivity is present in the indicator element or the diffusion element; and

G. means for placing and maintaining a biological specimen between the substrate element and the diffusion element whereby any urease in the biological specimen will react with the urea to generate ammonia which will permeate the diffusion membrane and be detected by the indicator element.

10. A test kit as in claim 9 wherein the substrate element matrix and the indicator element are attached to a common support member in a side by side relationship allowing one to be folded over onto the other.

11. A test kit as in claim 10 wherein the kit contains a holder or clamp for the common support member to be retained in a folded position.

12. A test kit as in claim 9 wherein urease is positioned on the diffusion element apart from the biological specimen position which urease acts as a positive control for the test kit.

13. A test kit as in claim 9 wherein the aqueous rehydrating solution and the buffer are combined to form a common solution.

14. A test kit as in claim 9 wherein the buffer is contained in the substrate element.

15. A test kit as in claim 9 wherein a predetermined amount of urease is placed on the diffusion element and acts as a positive control for the test kit.

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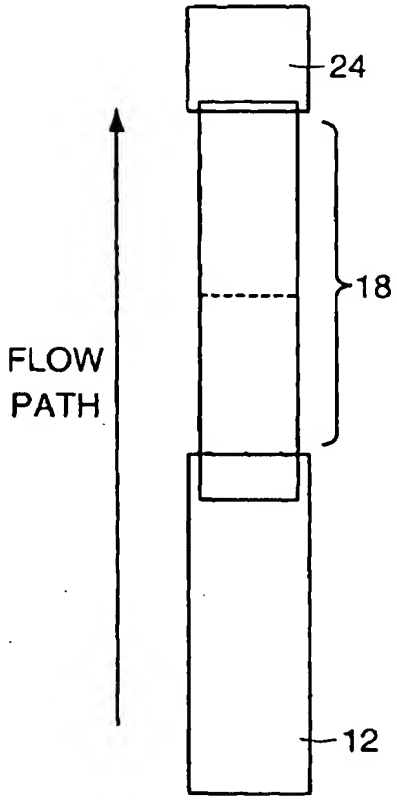

FIG. 2

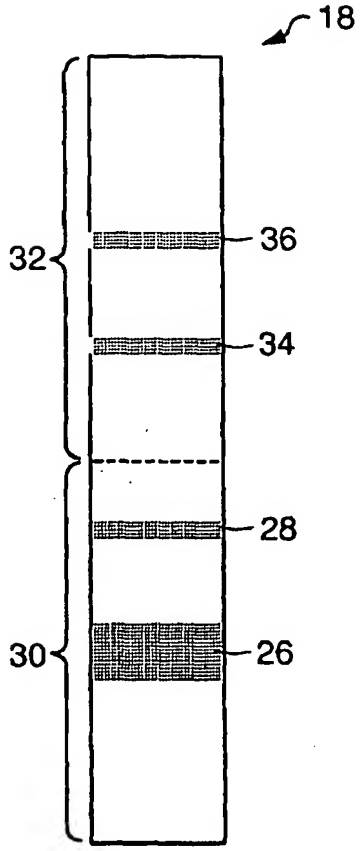

FIG. 3